A PROSPECTIVE STUDY OF MR SPECTROSCOPICAL AND POST OPERATIVE HISTOPATHOLOGICAL CORRELATION IN INTRA-CRANIAL SPACE OCCUPYING LESIONS

Dissertation

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CERTIFICATE

This is to certify that the dissertation titled "A PROSPECTIVE STUDY OF MR SPECTROSCOPICAL AND POST OPERATIVE HISTOPATHOLOGICAL CORRELATION IN INTRA CRANIAL SPACE OCCUPYING LESIONS" of Dr. Swarna Rekha Narayanan is in partial fulfillment of the requirements for M.Ch. Branch – II (Neurosurgery) Examination of the TamilNadu Dr. M.G.R. Medical University to be held in February 2009. The period of study was from Feb 2005 to Dec 2008 for 3 1/2yrs.

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DECLARATION

I, Dr. SWARNA REKHA NARAYANAN solemnly declare that dissertation titled, "A PROSPECTIVE STUDY OF MR SPECTROSCOPICAL AND POST OPERATIVE HISTOPATHOLOGICAL CORRELATION IN INTRA CRANIAL SPACE OCCUPYING LESIONS" is a bonafide work done by me at Govt. Stanley Medical College & Hospital during Feb 2005 to Dec 2008 for 3.5 yrs under the guidance and supervision of Prof. DILEEPAN MS (General Surgery) Professor and Head, Department of surgery & (IC) Neurosurgery.

The dissertation is submitted to TamilNadu, Dr. M.G.R. Medical University, towards partial fulfillment of requirement for the award of M.Ch. Neurosurgery (Branch – II).

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(Dr. SWARNA REKHA NARAYANAN)

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CONTENTS

I. INTRODUCTION

MR spectroscopy is a sequence in Magnetic Resonance Imaging which provides a measure of brain chemistry, a means of non invasive imaging that measures relative levels of various tissue metabolites. [1]

MRS, in the 1970s, involved phosphorus ^{31}P spectroscopy in animals, including evaluation of red blood cells and rat leg muscle tissue. Human application became possible in 1980s, when large bore magnets became available. The first human brain applications involved ^{31}P spectroscopy in infants. Bottmley and Radda and other co-authors then described applications of in vivo ^{31}P spectroscopy in the adult brain, followed in 1985 by the earliest in vivo brain hydrogen ^{1}H spectroscopic studies. [2]

The most common nuclei that are used are ^{1}H (proton), ^{23}Na (sodium), & ^{31}P (phosphorus). Proton spectroscopy is easier to perform and provides much higher signal-to-noise than either sodium or phosphorus. Proton MRS can be performed within 10-15 minutes and can be added on to conventional MR imaging protocols. It can be used to serially monitor biochemical changes in tumors, stroke, epilepsy, metabolic disorders, infections, and neurodegenerative diseases. Magnetic resonance spectroscopy allows noninvasive and in vivo exploration of the molecular composition of tissue. It identifies certain molecular constituents - the metabolites - involved in physiological or pathological processes.

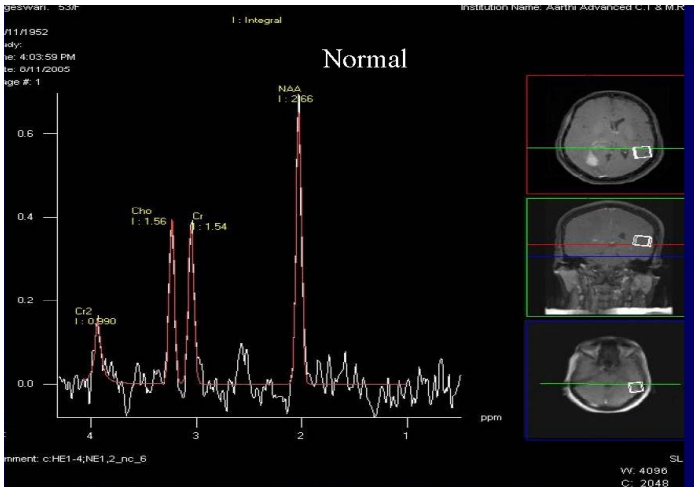
The important metabolites evaluated in long TE proton MR spectra are,

- N-Acetyl aspartate
- Choline
- Creatinine / phosphocreatinine
- Lactate

The important metabolites evaluated in short TE proton spectra (in addition to the above metabolites) are,

- Glutamate
- Glutamine
- Gamma-amino butyric acid
- Myo-Inositol
- Alanine
- Glucose
- Lipid [3]

The following picture shows proton spectra in the normal adult brain tissue in single voxel.



The above metabolites in various brain tumors were studied and the post op histopathology was correlated in this study.

II. AIM OF THE STUDY

To analyze the MR spectroscopy of the space occupying lesions in the brain with the post operative histopathology and try to find the reliability of MRS in making a pathological diagnosis pre operatively.

To analyze the spectroscopic diagnosis in association with parent images like CT brain (Plain & contrast) and conventional MRI (T1W,T2W & DWI) before giving the final imaging diagnosis.

To compare the results of our study with works available in the literature.

III. MATERIAL AND METHODS

This was a prospective study conducted in the department of Neurosurgery, Stanley Medical College, Chennai, during Feb 2005 – Dec 2008.

The 35 patients who presented with intracranial lesions diagnosed with CT Brain were done MRI & MR spectroscopy, where MRS pathological probable diagnosis was correlated with postoperative actual histopathological diagnosis of the lesion. For all the patients MRS was done using 1.5 Tesla magnets TE30 / TE136 / TE144 / TE270 using single voxel followed by resection of the SOL.

The space occupying lesions of more than 2 cm size was taken for the study.The total number of patients was 35 including 21 males, 10 females and 4 children.

SITE OF THE SOL:

Supratentorial lesions – 31 cases

Infra tentorial lesions - 4 cases

PROCEDURES PERFORMED:

Craniotomy and excision - 30

Suboccipital craniectomy & decompression of SOL - 4

Burr hole and tapping - 1

All patients were done suture removal on the 8th post operative day and discharged on 10th post operative day.

We could arrive at a probable pathological diagnosis of the lesions using MRI with the following findings.

- **Astrocytoma :**

Reduced NAA levels, moderately reduced Cr levels, and elevated Choline levels

Abnormally low NAA/Cr ratio & elevated Cho/Cr ratios

Elevated choline levels are seen more consistently in anaplastic astrocytomas than GBM.

Ependymomas display higher Cho/Cr ratios than those noted for astrocytomas in general.

Lactate levels may be elevated in all cysts regardless of etiology.

In highly vascular tumors lactate may be rapidly removed from the tumor and lactate spectra may not be present.

The presence of elevated lipid levels has also been used to differentiate low-grade from high-grade neoplasms, which is more specific for high grade tumor.

Lipids may originate from the tumor cells with in high grade astrocytomas, macrophages along the tumor periphery or areas of necrosis

- **Meningioma:**

Elevated alanine at 1.48 ppm is a signature of meningiomas.

The Cho/Cr ratio is higher in malignant meningiomas than in benign meningiomas

No lipid/ lactate.

- **Metastases :**

MRS of metastases is often nonspecific and indistinguishable from those of primary brain tumors.

But Lipid and lactate peak were more common with metastases than astrocytomas.

- **Radiation necrosis:**

Elevated lactate levels

No choline peak.

- **Hamartomas :**

NAA/Cho, NAA/Cr and Cr/Cho ratios in hamartomas are closer to those of normal brain tissue than to those of gliomas.

- **Bacterial Abscess:**

Acetate, succinate & Amino acid (alanine) peak in the cavity.

Cytosolic acid peak in the wall

Lipid peak inside the cavity

- **Tuberculoma:**

Prominent lipid resonances

Important peaks at the 1.3 and 0.9 ppm, corresponding to the methyl groups of fatty acid.

- **Lymphoma**:

Choline peak

Lipid lactate peak

- **Schwannoma:**

Absence of creatine, marked reduction in NAA, and increased lipids

- **Infarct :**

Decrease in NAA level, and lactate peak

- **Epidermoid:**

Lipid peak

The operated specimens were sent for Histopathological examination.

IV. RESULTS

The operated specimens were sent for Histopathological examination and the reports were compared with the pre operative MR Spectroscopical Data.

The following table showing the list of patients with MRS diagnosis and Histopathological Diagnosis

Total number of patients 35.

CASE NO	MRS DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS
1	LOW GRADE GLIOMA	GRADE 2 GLIOMA
2	ABSCESS	ABSCESS
3	GLIOMA	GRADE 3 GLIOMA
4	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
5	LOW GRADE GLIOMA	GRADE 1 GLIOMA
6	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
7	HIGH GRADE GLIOMA	LOW GRADE GLIOMA
8	LYMPHOMA	LYMPHOMA
9	INCONCLUSIVE	GANGLIOGLIOMA
10	LOW GRADE GLIOMA	PILOCYTIC ASTROCYTOMA
11	LOW GRADE GLIOMA	GRADE 2 GLIOMA
12	CRANIOPHARYNGIOMA	Grade 2 GLIOMA
13	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
14	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
15	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME

CASE NO	MRS DIAGNOSIS	HISTOPATHOLOGICAL DIAGNOSIS
16	HIGH GRADE GLIOMA	GRADE 3 GLIOMA
17	CEREBELLAR ABSCESS	CHRONIC ABSCESS
18	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
19	HIGH GRADE GLIOMA	GRADE 3 GLIOMA
20	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
21	INCONCLUSIVE	MENINGOTHELIAL MENINGIOMA
22	GLIOMA	TUBERCULOMA
23	HIGH GRADE GLIOMA	INFARCT
24	GLIOMA	MENINGIOMA
25	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
26	ABSCESS	MENINGIOMA
27	INCONCLUSIVE	GLIOMA
28	GLIOMA	MENINGIOMA
29	GLIOMA	LYMPHOMA
30	LOW GRADE GLIOMA	GRADE-2 GLIOMA
31	HIGH GRADE GLIOMA	SECONDARIES
32	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
33	EPIDERMOID	EPIDERMOID
34	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
35	ABSCESS	ABSCESS

The post op histopathology turned out to be Glioma in 22 patients , Meningioma in 4 patients, Abscess in 3,Lymphoma in 2, Tuberculoma in 1 patient, Epidermoid in 1 patient Metastatic secondaries in 1 patient ,and infarct in 1 patient.

The pre operative probable MRS pathological diagnosis was correlated with the post operative histopathology in 24 cases.

THE FOLLOWING TABLE SHOWING THE CORRELATED LIST OF PATIENTS

CASE NO	MRS DIAGNOSIS	HISTOPATHOLOGY REPORT
1	LOW GRADE GLIOMA	GRADE 2 GLIOMA
2	ABSCESS	ABSCESS
3	GLIOMA	GRADE 3 GLIOMA
4	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
5	LOW GRADE GLIOMA	GRADE 1 GLIOMA
6	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
7	HIGH GRADE GLIOMA	GRADE 2 GLIOMA
8	LYMPHOMA	LYMPHOMA
10	LOW GRADE GLIOMA	PILOCYTIC ASTROCYTOMA
11	LOW GRADE GLIOMA	GRADE 2 GLIOMA
13	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
14	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
15	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
16	HIGH GRADE GLIOMA	GRADE 3 GLIOMA
17	CEREBELLAR ABSCESS	CHRONIC ABSCESS
18	HIGH GRADE GLIOMA	GLIOBLASTOMA

CASE NO	MRS DIAGNOSIS	HISTOPATHOLOGY REPORT
		MULTIFORME
19	HIGH GRADE GLIOMA	GRADE 3 GLIOMA
20	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
25	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
30	LOW GRADE GLIOMA	GRADE-2 GLIOMA
32	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
33	EPIDERMOID	EPIDERMOID
34	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME
35	ABSCESS	ABSCESS

In Gliomas ,

The MRS diagnosis of a low grade Glioma was made in 6 cases and histopathology was also the same.

The MRS diagnosis of high grade Glioma was made in 13 patients and the histopathology was also the same.

In the 6 patients of low grade Glioma, the MRS diagnosis of high grade Glioma was made in one and the histopathology showed grade 2 Glioma.

The MRS diagnosis of abscess was made in 3 cases and the histopathology was also the same.

One case of lymphoma, one tuberculoma , and one epidermoid were also correlated with MRS diagnosis.

THE FOLLOWING TABLE SHOWING THE NON-CORRELATED LIST OF PATIENTS

CASE NO	MRS DIAGNOSIS	HISTOPATHOLOGY REPORT
9	INCONCLUSIVE	GANGLIOGLIOMA
12	CRANIOPHARYNGIOMA	GLIOMA
21	INCONCLUSIVE	MENINGOTHELIAL MENINGIOMA
22	GLIOMA	TUBERCULOMA
23	GLIOMA	INFARCT
24	GLIOMA	MENINGIOMA
26	ABSCESS	MENINGIOMA
27	INCONCLUSIVE	GLIOMA
28	GLIOMA	MENINGIOMA
29	HIGH GRADE GLIOMA	LYMPHOMA
31	HIGH GRADE GLIOMA	SECONDARIES

In 11 patients the MRS diagnosis was different or inconclusive.

In case-no 9 , the MRS was inclusive because of the extensive calcification in the lesion. The CT and conventional MRI gave the diagnosis of calcified lesion probably ganglioglioma. The post operative histopathology turned out to be ganglioglioma.

In case no 12; the MRS diagnosis was craniopharyngioma as the graph showed lipid peak and no choline peak. But the post operative histopathology turned out to be a glioma.

In case no 21, the MRS diagnosis was inconclusive due to calcifications. The post operative histopathology was meningioma.

In case no 22, the MRS diagnosis was glioma as the graph showed choline peak and no lipid or lactate trace. But the post operative histopathology was tuberculoma.

In case no 23, the MRS diagnosis was glioma as the graph showed both choline and lipid peak. But the post operative histopathology was an infarct.

In case no 23, although the CT , and conventional MRI pictures gave the diagnosis of meningioma, the MRS graph showed the choline peak and the MRS diagnosis was Glioma. But the histopathology was meningioma.

In case no 24, the MRS diagnosis was abscess as the graph showed alanine peak. But the intra operative and histopathology diagnosis was meningioma.

In case no 27, as the MRS gave irregular graphs the MRS diagnosis was given as teratoma. The histopathology turned out to be glioma.

In case no 28, an intraventricular SOL , as it showed choline peak and no alanine trace, the MRS diagnosis was glioma. But the post operative histopathology was turned out to be meningioma.

In case no 29, a double lesion in thalamic and occipital region, MRS diagnosis was high grade glioma, but the histopathology turned out to be lymphoma.

In case no 31 , because the tumor showed choline and lipid peak the diagnosis of high grade glioma was given and the histopathology turned out to be a secondary deposit from carcinoma lung.

V. ANALYSIS

In the total number of 35 patients, 24 patients correlated and 11 patients did not correlate with the MRS diagnosis.

In Gliomas,

MRS diagnosis and histopathological diagnosis were same in 19 patients. These patients showed typical of glioma traces in MRS including reduced NAA levels, moderately reduced Cr levels, and elevated Choline levels. High grade gliomas showed lipid lactate peak along with the above features. In one patient the MRS diagnosis was high grade glioma as there was associated lactate peak. But the histopathology turned out to be low grade glioma.

MRS diagnosis of non Glioma but histopathologically of Glioma was made in 3 patients. In one patient with lesion in left temporal region with calcifications, the graphs were distorted and multiple with no significant peak. The histopathology was ganglioglioma. In another patient lesion showed lipid peak without choline peak in a suprasellar region. It was diagnosed as craniopharyngioma but the histopathology was turned out to be glioma. In one patient with pineal region cystic SOL, the MRS showed inconclusive graphs. Tumor was thought to be teratoma but the histopathology was glioma.

The MRS diagnosis of Glioma and histopathologically of non Glioma was present in 6 patients. This includes 2 meningiomas, a tuberculoma, an infarct, a lymphoma and a secondary deposit. All these patients showed choline peak with or without lipid peak

without the typical MRS features of the respective histopathology.

In meningiomas,

MRS diagnosis of meningioma was not made, but the post operative histopathology of meningioma was seen in 4 patients who were diagnosed by MRS as glioma in one, abscess in one and the graphs were inconclusive in 2 due to calcification.

In the 1st patient it showed choline peak, in the second one it showed alanine but at that time period (2006) it was indicative of an abscess and diagnosis of abscess was made. In the last 2 patients because of the calcification seen in meningiomas the graphs were inconclusive. When we correlate the clinical, CT and Conventional MRI the diagnosis of meningioma could be made.

In Lymphomas,

2 cases were proved to be lymphomas histopathologically. One patient correlated with MRS and the other patient's MRS diagnosis was suggestive of high grade glioma. In the non corrlelated patient when we correlate with clinical,CT, and conventional MRI with multiplicity of the lesion the diagnosis of lymphoma could be arrived.

In Abscess,

MRS diagosis correlated well with histopathology. But in one patient the MRS diagnosis was abscess and histopathology was meningioma.

In Epidermoid MRS correlated well with histopathology. MRS showed a

prominent lipid peak.

In a Tuberculoma , MRS diagnosis of Glioma was made due to the choline peak which was misleading.

In a case of infarct because of the choline peak and lipid peak it was thought to be a glioma.

In a secondary deposit from carcinoma lung, the MRS diagnosis was high grade glioma as there was choline and lactate peak.

In one patient of proved low grade glioma, the MRS diagnosis of craniopharyngioma was given as it showed a lipid peak with out choline peak.

When correlating the Clinical features, CT,Conventional MRI along with MRS the histopathological diagnosis could be arrived to a reasonable level.

THE FOLLOWING TABLE SHOWING THE MRS DIAGNOSIS , DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS AND HISTOPATHOLOGICAL DIAGNOSIS FOR ALL 35 PATIENTS

CASE NO	**MRS DIAGNOSIS**	**DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS**	**HISTOPA-THOLOGY REPORT**
1	LOW GRADE GLIOMA	LOW GRADE GLIOMA	GRADE 2 GLIOMA
2	ABSCESS	ABSCESS	ABSCESS

CASE NO	MRS DIAGNOSIS	DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS	HISTOPA-THOLOGY REPORT
3	GLIOMA	GLIOMATOSIS CEREBRI	GRADE 3 GLIOMA
4	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
5	LOW GRADE GLIOMA	LOW GRADE GLIOMA	GRADE 1 GLIOMA
6	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
7	HIGH GRADE GLIOMA	LOW GRADE GLIOMA	LOW GRADE GLIOMA
8	LYMPHOMA	LYMPHOMA	LYMPHOMA
9	INCONCLUSIVE	GANGLIOGLIOMA	GANGLIOGLIOMA
10	LOW GRADE GLIOMA	LOW GRADE GLIOMA	PILOCYTIC ASTROCYTOMA
11	LOW GRADE GLIOMA	LOW GRADE GLIOMA	GRADE 2 GLIOMA
12	CRANIOPHARYNGIOMA	CRANIOPHARYNGIOMA	Grade 2 GLIOMA
13	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
14	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
15	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
16	HIGH GRADE GLIOMA	GRADE 3 GLIOMA	GRADE 3 GLIOMA

CASE NO	MRS DIAGNOSIS	DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS	HISTOPA-THOLOGY REPORT
17	CEREBELLAR ABSCESS	CHRONIC ABSCESS	CHRONIC ABSCESS
18	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
19	HIGH GRADE GLIOMA	HIGH GRADE GLIOMA	GRADE 3 GLIOMA
20	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
21	INCONCLUSIVE	MENINGIOMA	MENINGIOMA
22	GLIOMA	TUBERCULOMA	TUBERCULOMA
23	GLIOMA	HIGH GRADE GLIOMA	INFARCT
24	GLIOMA	MENINGIOMA	MENINGIOMA
25	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
26	ABSCESS / MENINGIOMA	MENINGIOMA	MENINGIOMA
27	INCONCLUSIVE	TERATOMA	GLIOMA
28	GLIOMA	MENINGIOMA	MENINGIOMA
29	GLIOMA	LYMPHOMA	LYMPHOMA
30	LOW GRADE GLIOMA	GRADE-2 GLIOMA	GRADE-2 GLIOMA
31	HIGH GRADE GLIOMA	SECONDARIES	SECONDARIES
32	HIGH GRADE GLIOMA	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME

CASE NO	MRS DIAGNOSIS	DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS	HISTOPA-THOLOGY REPORT
33	EPIDERMOID	EPIDERMOID	EPIDERMOID
34	HIGH GRADE GLIOMA	GLIOBLASTOMA MULTIFORME	GLIOBLASTOMA MULTIFORME
35	ABSCESS	ABSCESS	ABSCESS

THE FOLLOWING TABLE INDICATES THE LIST OF PATIENTS WHERE THE FINAL DIAGNOSIS IMPROVED IN WHOM WHICH WERE NON CORRELATING BEFORE.

SL. NO	MRS DIAGNOSIS	DIAGNOSIS WITH CLINICAL FEATURES, CT,CONVENTIONAL MRI ALONG WITH MRS	HISTOPA-THOLOGY REPORT
9	INCONCLUSIVE	GANGLIOGLIOMA	GANGLIOGLIOMA
12	CRANIO PHARYNGIOMA	CRANIO PHARYNGIOMA	GLIOMA
21	INCONCLUSIVE	MENINGIOMA	MENINGIOMA
22	GLIOMA	GLIOMA	TUBERCULOMA
23	GLIOMA	GLIOMA	INFARCT
24	GLIOMA	MENINGIOMA	MENINGIOMA
26	ABSCESS / MENINGIOMA	MENINGIOMA	MENINGIOMA
27	INCONCLUSIVE	TERATOMA	GLIOMA
28	GLIOMA	MENINGIOMA	MENINGIOMA
29	HIGH GRADE GLIOMA	LYMPHOMA	LYMPHOMA
31	HIGH GRADE GLIOMA	HIGHGRADE GLIOMA	SECONDARIES

The final pre operative histopathological diagnosis could be made in all the meningiomas, a ganglioglioma and in a lymphoma. But the diagnosis didn’t alter in 5 patients even after correlating with the clinical, CT, Conventional MRI and MRS.

We could assess the respective post operative histopathological diagnosis in 24/35

patients pre operatively when taking the MRS alone in to account. But after correlating with patient's clinical features, CT, Conventional MRI and MRS, the pre operative histopathological diagnosis was made in 30/35. But still 5 patients were not correlating with the post operative Histopathology.

VI. STATISTICS

Total number of cases -35

Post op Histopathological report :

Gliomas – 22

Meningiomas-4

Lymphomas-2

Abscess-3

Tuberculoma-1

Epidermoid 1

Secondaries -1

Infarct -1

The cases for which MRS correlated with histopathology:

Total -24

Glioma - 19

Low grade – 6

High grade -13

Abscess -3

Lymphoma – 1

Meningioma-0

Epidermoid-1

MRS AND HPE CORRELATED – 24 PATIENTS

P VALUE – 0.028 *

Tumor wise correlation:

Gliomas:

Total Gliomas - 22

MRS Glioma & HPE glioma -19

MRS Non-glioma & HPE glioma – 3

MRS Glioma & HPE non glioma – 6

Sensitivity – 86.4%

Specificity – 53.8%

P value – 0.011 *

Meningioma:

Total Meningiomas - 4

MRS Meningioma & HPE Meningioma -0

MRS Non-meningioma & HPE Meningioma -4

MRS Meningioma & HPE non-Meningioma -0

Statistics can not be applied as there is no true positive cases.

Abscess:

Total abscesses – 4

MRS Abscess & HPE Abscess -3

MRS Non Abscess & HPE abscess -0

MRS Abscess & HPE Non abscess -1

Statistics :

Sensitivity -100%

Specificity –96.9%

P value - < 0.001**

Lymphomas:

Total lymphomas – 2

MRS Lymphoma + HPE lymphoma -1

MRS Non lymphoma + HPE Lymphoma -1

MRS Lymphoma + HPE non lymphoma -0

Statistics:

Sensitivity -50%

Specificity –100%

P value - < 0.001**

Epidermoid:

Total Epidermoid – 1

MRS Epidermoid + HPE Epidermoid -1

MRS Non Epidermoid + HPE Epidermoid -0

MRS Epidermoid + HPE non Epidermoid -0

Sensitivity – 100%

Specificity – 100%

P value - < 0.001**

As there are no true positive cases the statical value can not be obtained for tuberculoma, secondary metastasis and infarct.

After correlating with clinical features, CT Brain plain with contrast, Conventional MRI and MRS the total number of patients who correlated with the post operative histopathology increased. But still 5 patients were not correlating.

Only with MRS - 24/35

P value – 0.028*

Along with clinical features, CT Brain plain with contrast, Conventional MRI And MRS - 30/35

P value - < 0.001**

* Denotes significant at 1% level

**Denotes significant at 5% level

VII. DISCUSSION

Proton MRS can improve the diagnostic accuracy preoperatively in brain tumors and help in monitoring the response to surgical, medical and radiation management. In MRS, changing the TE , changes the type of information obtained as well as the appearance of the frequency domain spectrum. Different TE can be used for obtaining MR spectra of brain tumors. In this study different TE (30 ms, 136ms, 144 ms &270ms) were used. Short TE provides slightly better tumor classification, and results improve when both short and long TE are considered simultaneously. Meningioma is the only tumor group in which long TE performed better than short TE. With a short TE of 30 msec, metabolites with both short and long T2 relaxation times are observed. With a long TE of 270 msec, only metabolites with long T2 relaxation times are seen, producing a spectrum with primarily NAA, creatine, and choline. One other helpful TE is 144 msec where inverts lactate at 1.3 ppm.

2 types of MRS are available. Single voxel and multi-voxel. As a general rule, the single voxel, short TE technique is used to make the initial diagnosis, because the signal-to-noise is high and all metabolites are represented. Multi-voxel, long TE techniques are used to further characterize different regions of a mass and to assess brain parenchyma around or adjacent to the mass. Multi-voxel, long TE techniques are also used to assess response to therapy and to search for tumor recurrence. Multi-voxel spectroscopy is best to detect infiltration of malignant cells beyond the enhancing margins of tumors. Particularly in the case of cerebral glioma, elevated choline levels are frequently detected in edematous regions of the brain outside the enhancing mass.

The important metabolites evaluated in long TE proton MR spectra are,

- N-Acetyl aspartate
- Choline
- Creatinine / phosphocreatinine
- Lactate

The important metabolites evaluated in short TE proton spectra(in addition to the above metabolites) are,

- Glutamate
- Glutamine
- Gamma-amino butyric acid
- Myo-Inositol
- Alanine
- Glucose
- Lipid

Most proton spectra today are described in terms of metabolite ratio, with creatinine often used as the reference standard.

Metabolites and their significance:

Sl. no	metabolite	PPM	Normal value	Contributions from	How it is produced	Significance	Physiologically increased	Physiological lydecreased	Pathologically Increased	Pathologically Decreased
1	NAA	2.01	8-9 mmol/kg	N-Acetyl groups, N-Acetyl aspartylglutamate, glycoproteins& aminoacid residues in peptides	Synthesized in the mitochondria from aspartate and acetyl CoA .	Peak Indicates Normal neuronal activity that is the presence of intact glioneural structures.	Normal gray mater – adults Normal gray mater - infants Normal white mater - infants	Normal White mater- adults	Canavan's disease	Neuronal loss-neurodegenerative disease,stroke, brain tumors, epilepsy, & multiple sclerosis
2	Creatine	3.03 & 3.94	7.5mmol/kg	Methyl protons of creatine& phosphocreatine. Minor contribution-GABA,Lysine&Glutathione	Present in neurons as a buffer in cellular ATP-ADP reservoirs	Indirect indicator of brain intracellular energy stores. Peak is used as an internal reference standard for characterizing other metabolite signal intensities.	Normal white mater	Normal cerebellum		Malignant Brain tumors
3	Choline	3.2	1.32 mmol/kg	Trimethylammonium residues of free choline ,phosphocholine, phosphatidylcholine and glycerophosphocholine	Present in all processes resulting in hypercellularity(primary brain neoplasm/gliosis) or myelin breakdown(demyelinating disease)	Peak reflects cell membrane synthesis&degradation			Primary brain neoplasms, demyelinating disease	Hypomyelinating disease
4	Myo-inositol	3.56 & 4.06	6.56 mmol/kg	MI-Monophosphate & glycine	Present in glial cells absent in neurons. The role in osmotic regulation of the brain has been attributed to MI.	It's glial marker			Demyelinating disease & Alzheimer's disease	Hepatic encephalopathy

Sl. no	metabolite	PPM	Normal value	Contributions from	How it is produced	Significance	Physiologically increased	Physiological lydecreased	Pathologically Increased	Pathologically Decreased
5	Lactate	Doublet in 1.32 seperated by 0.2ppm & also in 4.1	Absent or <0.5 mmol/L		Nonspecific indicator of anaerobis glycolysis Rate of washout of the lactate from the tumor tissue depends on the vascularity.	Peak is a nonspecific indicator of anaerobic glycolysis			Brain neoplasms – rapidly growing with vascular jeopardisation. ,infarcts,hypoxia,metabolic disorders or seizures	
6	Glutamate, Glutamine, and GABA	2.1 & 2.5		Glutamate, glutamine & GABA	Present in neurons as neurotransmitters				Increased in schizophrenia and epilepsy	
7	Alanine	1.3 & 1.5		Alanine					Increased in meningiomas, central neurocytoma	
8	Lipid	1.2–1.4		Free fatty acids		Necrosis				
9	Cytosolic acid			Amino acid					Bacterial abscess	

Basic facts about the metabolites in normal brain:

- NAA is present in very low concentration in the newborn brain, compared to those in the adult brain, but levels rapidly increase during the first 2-3yrs of life.
- Pre term infants were noted to have lower brain NAA levels than full-term infants.
- Myo-inositol forms the most prominent peak in the newborn indicating the presence of active myelination.
- NAA & Cr levels increase during the first few weeks of life, Cho and MI levels decrease.
- The Cr/Cho ratio increases in gray matter during the first 2 years of life, whereas the ratio remains nearly constant in white matter.
- Lactate peaks are normally seen in preterm and small-for-gestational-age infants.
- In the developing brain, proton MR spectra demonstrate that different parts of brain mature at different rates and at different times and the more metabolically mature areas demonstrate lower MI and higher NAA levels than those in less mature regions of the brain. Specifically, the basal ganglia, perirolandic cortex, and visual cortex mature before areas such as prefrontal cortex and

temporal cortex.

- Spectral pattern stabilizes in early adulthood, and NAA level begins to decrease with advancing age.

Brain tumors:

MRS can be used to determine the degree of malignancy. As a general rule, as malignancy increases, NAA and creatine decrease, and choline, lactate, and lipids increase. NAA decreases as tumor growth displaces or destroys neurons. Highly malignant tumors have high metabolic activity and deplete the energy stores, resulting in reduced creatine. Hypercellular tumors with rapid growth elevate the choline levels. Lipids are found in necrotic portions of tumors, and lactate appears when tumors outgrow their blood supply and start utilizing anaerobic glycolysis. To get an accurate assessment of the tumor chemistry, the spectroscopic voxel should be placed over an enhancing region of the tumor, avoiding areas of necrosis, hemorrhage, calcification, or cysts.

The common way to analyze clinical spectra is to look at metabolite ratios, namely NAA/Cr, NAA/Cho, and Cho/Cr. Normal and abnormal values are shown in the table. By including a known reference solution when acquiring the MR spectral data, absolute concentrations of metabolites can be calculated. But nowadays the ratios are not used as

there is not much of significance. When the brain becomes ischemic, it switches to anaerobic glycolysis and lactate accumulates. Markedly elevated lactate is the key spectroscopic feature of cerebral hypoxia and ischemia. If cerebral infarction ensues, lipids increase.

As in the case of non-glial tumors, brain abscesses destroy or displace brain tissue, so NAA is not present. The voxel should include the abscess cavity to detect the breakdown products of these lesions. Lactate, cytosolic acid, alanine, and acetate are characteristic metabolites in bacterial abscesses. Toxoplasmosis and tuberculomas show prominent peaks from lactate and lipids.

There is also considerable interest in using MRS to distinguish the common focal brain lesions in AIDS patients. The most helpful marker is choline, which is elevated in lymphoma, but low or absent in toxoplasmosis, tuberuloma, and cryptococcoma. Toxoplasmosis is characterized by markedly increased lactate and lipids and depletion of normal brain metabolites. Tuberculoma and cryptococcoma are similar but with relatively little lactate.

In the initial period the ratios were used and as there were lots of variation it is not used nowadays. Rather the individual metabolites in multivoxel provides significance results.

A common clinical problem is distinguishing tumor recurrence from radiation effects several months following surgery and radiation therapy. Elevated choline is a marker for recurrent tumor. Radiation change generally exhibits low NAA, creatine, and choline on spectroscopy. If radiation necrosis is present, the spectrum may reveal elevated lipids and lactate.

Most non-glial tumors have little or no NAA. They also have very low creatine, and elevated glutamates

Finally, MRS can direct the surgeon to the most metabolically active part of the tumor for biopsy to obtain accurate grading of the malignancy.

Advantages :

- It can be done with the conventional MRI.
- Takes 10-15 mins to complete the imaging which is non invasive.

Disadvantages:

- Small lesions of less than 2cms can not be assessed. Voxel contamination is more.

- Cystic lesions produce sampling error. And also the lesions near bone, CSF, or blood produce sampling error.

- Calcifications in the lesion could cause inappropriate peaks and gives inconclusive pictures.

- Theoretically, NAA is not present in the meningiomas. But in clinical experience it is not uncommon to detect NAA in these extra axial tumors. The reason for the presence of NAA in these tumors may be contamination of the voxel by adjacent normal brain parenchyma, use of large voxel , or inadequate voxel placement.

- Although in theory NAA should not be present in metastases because of their lack of neural or glial components, it frequently is present in proton MR spectra, presumably secondary to voxel comtamination with adjacent brain parenchyma or due to the presence of N-acetylated metabolites on their cell membranes.

VIII. CONCLUSION

- When diagnostic dilemmas present themselves, MR spectroscopy considered in perspective with MR imaging and clinicopathologic features can be useful in certain situations.

- MRS study does increase specificity, and may help in improving our ability to predict pre operative histological diagnosis.

- MRS can help increase ability to predict grade of the Glioma. As the grade increases NAA and creatine decrease and choline, lipids and lactate increase.

- When correlating with the clinical features, CT and Conventional images , the probable pathological diagnosis can be obtained up to 85%.

IX. REVIEW OF THE LITERATURE

Shimizu and associates demonstrated that high grade brain tumors were associated with higher Cho/reference and lower NAA/reference values in their series.[3]

In their series of 27 patients with biopsy confirmed brain tumors, Meyerand and colleagues showed that the combination of lac/water and choline/water ratio obtained from regions of contrast enhancing brain tumors permitted differentiation of low grade astrocytomas from anaplastic astrocytomas and Glioblastoma Multiforme(GBM). [3]

In a multi centre study involving 86 cases of glial tumors, megendank and coauthors showed that all tumors demonstrated abnormally decreased NAA/Cr and increased Cho/Cr ratios with respect to normal brain parenchyma.[4]

Butcher and colleagues have described a series of 26 intracranial tumors in which MRS allowed differentiation of infiltrative processes from circumscribed lesions but did not allow differentiation of different types of lesions with in each category.[4]

Kinoshiotal and colleagues suggested that glycine levels were markedly elevated in GBMs, high-grade astrocytomas, ependymomas and medulloblastomas, whereas they were low in metastatic tumors.[4]

One study involving 25 patients with cerebral astrocytomas who received a combination of radiation and chemotherapy demonstrated increased.[4]

Grand and co workers, in their series of 34 cystic intracranial lesions, showed that a TE of 136 msec, the detection of an aminoacid resonance at 0.9 ppm in bacterial abscess allows differentiation from necrotic neoplasms, which donot show this specral peak. [3]

Similar studies in the recent past

1. Noninvasive Evaluation of Malignancy of Brain Tumors with Proton MR Spectroscopy – AJNR Apr *AJNR Am J Neuroradiol* 17:737–747, April 1996

Water-suppressed single-voxel point resolved spectroscopy in the frontal white matter of 17 healthy volunteers and 25 patients with brain tumors yielded spectra with peaks of *N*-acetyl aspartate (NAA), choline-containing compounds (Cho), creatine/phosphocreatine (Cre), and lactate. These peak intensities were semiquantitated as a ratio to that of the external reference. The validity of the semiquantitation was first evaluated through phantom and volunteer experiments. The variation in measurements of the designated region in the volunteers was less than 10%. Normal ranges of NAA/reference, Cho/reference, and Cre/reference were 3.596 0.68, 1.96 6 0.66, and 1.53 6 0.64 (mean 6 SD), respectively.

In 17 gliomas, the Cho/reference value in high-grade gliomas was significantly higher than in low-grade gliomas. Levels of NAA/ reference were also significantly different in low-grade and high-grade malignancy. In eight meningiomas (four newly diagnosed and four recurrent), the level of Cho/reference was significantlyhigher in recurrent meningiomas than in normal white matter or in newly diagnosed meningiomas. Higher grades of brain tumors in this study were associated with higher Cho reference and lower NAA reference values. These results suggest that clinical proton MR spectroscopy may help predict tumor malignancy.

2. Role of in vivo proton MR Spectroscopy in the evaluation of adult brain lesions – Neurology India October-december 2003

3. Comparison between neuroimaging classifications and histopathological diagnoses using an international multicenter brain tumor magnetic resonance imaging database - **J Neurosurg 105:**6–14, 2006

The authors retrospectively assessed the correlation between neuroimaging classifications and histopathologicaldiagnoses by using multicenter database records from 393 patients with brain tumors. An ontology was devised to establish diagnostic agreement. Each tumor category was compared with the corresponding histopathological diagnoses by dichotomization. Sensitivity, specificity, positive and negative predictive values (PPVs and NPVs, respectively),and the Wilson

95% confidence intervals (CI) for each were calculated. In routine reporting of MR imaging examinations, tumor types and grades were classified with a high specificity (85.2–100%); sensitivity varied, depending on the tumor type and grade, alone or in combination. The recognition of broad diagnostic categories (neuroepithelial or meningeal lesions) was highly sensitive, whereas when both detailed type and grade were considered, sensitivity diverged, being highest in low-grade meningioma (sensitivity 100%, 95% CI 96.2–100.0%) and lowest in high-grade meningioma (sensitivity 0.0%, 95% CI 0.0–65.8%) and low-grade oligodendroglioma (sensitivity 15%, 95% CI 5.2–36.0%). In neuroepithelial tumors, sensitivity was inversely related to the precision in reporting of grade and cellular origin; “glioma” was a frequent neuroimaging classification associated with higher sensitivity in the corresponding category. The PPVs varied among categories, in general being greater than their prevalence in this dataset. The NPV was high in all categories (69.8–100%).

The PPVs and NPVs provided in this study may be used as estimates of posttest probabilities of diagnostic accuracy using MR imaging. This study targets the need for noninvasively increasing sensitivity in categorizing most brain tumor types while retaining high specificity, especially in the differentiation of high- and low-grade glial tumor classes.

4. Proton magnetic resonance spectroscopy and diffusion-weighted imaging in intracranial cystic mass lesions. -***Surg Neurol. 2007;68 Suppl 1:S25-36***

The differential diagnosis of various intracranial cystic lesions is sometimes difficult on the basis of CT or MRI findings. Our objective was to evaluate (1)H MRS and DWI in the differential diagnosis of these lesions and in comparison with conventional MRI. METHODS: Fifty patients with intracranial cystic lesions (21 pyogenic abscesses, 23 tumor cysts, 3 epidermoid cysts, and 3 arachnoid cysts) were evaluated with conventional MRI, DWI, and in vivo (1)H MRS. Preoperative diagnosis of the lesions was based on the results of DWI and in vivo MRS. All DWI and (1)H MRS studies were performed with a clinical 1.5-T system. The DWI was performed using single-shot spin-echo echo-planar pulse sequence with b = 1000 s/mm(2). The ADC value was measured. Diagnostic accuracy of conventional MRI, DWI, and in vivo (1)H MRS was calculated with respect to a final diagnosis of brain abscess vs nonabscess cystic tumor.

Lactate and cytosolic amino acids with/without succinate, acetate, and alanine were observed in 18 of 21 cases of abscesses on MRS. In 3 cases of epidermoid cysts, lactate was observed and could be differentiated from 3 cases of arachnoid cysts, which showed only minimal lactate. Only lactate was seen in 14 of 23 patients with tumor cysts, whereas both lipid/lactate and choline were visible in 9 patients with tumor cysts. Increased signal was seen in 20 of 21 patients with abscesses and 3 patients with epidermoid cysts on DWI. Decreased signal was observed in 22 of 23 patients with tumor cysts and 3 patients with arachnoid cyst on DWI. Diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of conventional MRI for the differentiation of brain abscess from nonabscess cystic tumor were 61.4%, 61.9%, 60.9%, 59.1%, and 63.6%, respectively, whereas they were 93.2%, 85.7%, 100%, 100%, and 88.5% with MRS; 95.5%, 95.2%, 95.7%, 95.2%, and 95.7% with DWI; and 97.7%, 95.2%, 100%, 100%, and 95.8% with MRS and DWI. Magnetic resonance imaging, when combined with in vivo MRS and DWI, accurately predicted the diagnosis in 47 (94%) of 50 and 48 (96%) of 50 of the cases, respectively. Proton MRS and DWI are useful as additional diagnostic modalities in differentiating intracranial cystic lesions. Combination of DWI with calculated ADC values and metabolite spectrum acquired by MRS add more information to MRI in the differentiation of intracranial cystic mass lesions

5. Correlation of magnetic resonance spectroscopic and growth characteristics within Grades II and III gliomas-J Neurosurg 106:660–666, 2007

The accurate diagnosis of World Health Organization Grades II and III gliomas is crucial for the effective treatment of patients with such lesions. Increased cell density and mitotic activity are histological features that distinguish Grade III from Grade II gliomas. Because increased cellular proliferation and density both contribute to the in vivo magnetic resonance (MR) spectroscopic peak corresponding to choline-containing compounds (Cho), the authors hypothesized that multivoxel MR spectroscopy might help identify the tumor regions with the most aggressive growth characteristics, which would be optimal locations for biopsy. They investigated the ability to use one or more MR spectroscopic parameters to predict the MIB-1 cell proliferation index (PI), the terminal deoxynucleotidyl transferase–mediated deoxyuridine triphosphate nick-end labeling cell death index (DI), the cell density, and the ratio of proliferation to cell death (PI/DI) within different regions of the same tumor.

Patients with presumed Grades II or III glioma underwent 3D MR spectroscopic imaging prior to surgery, and two or three regions within the tumor were targeted for biopsy retrieval based on their spectroscopic

features. Biopsy specimens were extracted from the tumor during image-guided resection, and the PI, DI, and cell density were assessed in the specimens using immunohistochemical methods.

The authors found that the relative levels of Cho and *N*-acetylaspartate (NAA) correlated with the cell density, PI, and PI/DI ratio within different regions of the same tumor and that the association held for the subpopulation of nonenhancing tumors. The association was stronger in tumors with large ranges of Cho/ NAA values, irrespective of the presence of contrast enhancement. The findings demonstrate the validity of using MR spectroscopy to identify regions of aggressive growth in presumed Grade II or III gliomas that would be suitable targets for retrieving diagnostic biopsy specimens.

6. Increase in glutamate as a sensitive indicator of extracellular matrix integrity in peritumoral edema: a 3.0-tesla proton magnetic resonance spectroscopy study - J Neurosurg 106:609–613, 2007

The authors of previous studies based on diffusion tensor imaging have indicated that there are two types of peritumoral edema—namely, edema with preserved structural integrity of the glial matrix and edema with compromised glial matrix. The authors of this study hypothesized that functionality of the glutamate (Glu)–glutamine shuttle, a vital neuron–glia interaction, may be differentially affected by peritumoral edema. They tested this hypothesis using proton magnetic resonance

(MR) spectroscopy on a 3.0-tesla system that is capable of quantifying Glu without need of editing.

Twenty-three patients, each with a single brain tumor mass and peritumoral edema (nine high-grade gliomas, eight metastatic brain tumors, and six meningiomas), and nine healthy individuals participated in this study. Single-voxel proton MR imaging targeting the region of peritumoral edema was performed using a 3.0-tesla system.

Glutamate levels in the peritumoral edema of nonglial tumors was significantly elevated (p , 0.01) compared with edema associated with glial tumors or normal white matter. The finding confirmed that peritumoral edema in nonglial tumors is distinct from that of glial tumors, as previously indicated in diffusion tensor imaging studies. The authors hypothesized that the former condition represents a compensatory increase in activities of the Glu–glutamine shuttle brought about by simple expansion of the extracellular space due to edema. The assessment of Glu concentrations in peritumoral edema using 3.0-tesla proton MR spectroscopy may be developed into an objective index of the structural integrity of the glial matrix.

7. Comparative Evaluation of Fungal, Tubercular, and Pyogenic Brain Abscesses with Conventional and Diffusion MR Imaging and Proton MR Spectroscopy - AJNR 28 , Aug 2007

It is difficult to differentiate the cause of brain abscesses with the use of CT and MR imaging. The author did a comparative evaluation of pyogenic, tubercular, and fungal brain abscesses by using conventional, diffusion-weighted imaging (DWI), and proton MR spectroscopy (PMRS) with an aim to define the unique features that may differentiate among the pyogenic, tubercular, and fungal brain abscesses.

They have performed a retrospective analysis on 110 patients with surgically proved brain abscesses. Imaging studies included T2, T1, postcontrast T1, DWI, and PMRS. Apparent diffusion coefficient (ADC) of the wall and cavity of the abscesses were quantified. The morphologic, physiologic, and metabolite features of pyogenic (*n*_91), tubercular (*n*_11), and fungal (*n*_8) abscesses were compared.

The pyogenic abscesses had smooth (55/91) and lobulated (36/91) walls, whereas the tubercular abscesses had smooth (4/11), lobulated (6/11), or crenated walls (1/11) with no intracavitary projections. The fungal abscesses showed irregular walls (lobulated 4/8, crenated 4/8) with intracavitary projections (8/8). The wall as well as the cavity showed low ADC in the pyogenic and tubercular abscesses. In the fungal abscesses, the wall and projections showed low ADC (8/8); however, the cavity

itself showed high ADC (8/8). PMRS showed cytosolic amino acids (89/91), acetate (25/91), and succinate (18/91) in the pyogenic abscesses, whereas lipid/lactate (11/11) was seen in the tubercular abscesses. The fungal abscesses showed lipid (4/8), lactate (7/8), amino acids (4/8), and multiple peaks between 3.6 and 3.8 ppm assigned to trehalose (5/8).

Based on the morphologic, ADC, and metabolite information, it may be possible to differentiate among the pyogenic, tubercular, and fungal brain abscesses.

8. Proton magnetic resonance spectroscopy in pituitary macroadenomas: preliminary results - J Neurosurg 109: 2008

The aim of this study was to correlate proton MR (1H-MR) spectroscopy data with histopathological and surgical findings of proliferation and hemorrhage in pituitary macroadenomas. point-resolved spectroscopy sequence (TR 2000 msec, TE 135 msec) with 128 averages and chemical shift selective pulses for water suppression was used. Voxel dimensions were adapted to ensure that the volume of interest was fully located within the lesion and to obtain optimal homogeneity of the magnetic field. In addition, water- unsuppressed spectra (16 averages) were acquired from the same volume of interest for eddy current correction, absolute quantification of metabolite signals, and determination of full width at half maximum of the unsuppressed water peak (FWHMwater).

Metabolite concentrations of choline-containing compounds (Cho) were computed using the LCModel program and correlated with MIB-1 as a proliferative cell index from a tissue specimen.In 16 patients harboring macroadenomas without hemorrhage, there was a strong positive linear correlation between metabolite concentrations of Cho and the MIB-1 proliferative cell index ($R = 0.819$, $p < 0.001$). The metabolite concentrations of Cho ranged from 1.8 to 5.2 mM, and the FWHMwater was 4.4–11.7 Hz. Eleven patients had a hemorrhagic adenoma and showed no assignable metabolite concentration of Cho, and the FWHMwater was 13.4–24.4 Hz. In 10 patients the size of the lesion was too small (< 20 mm in 2 directions) for the acquisition of MR spectroscopy data.

The conclusion made was Quantitative 1H-MR spectroscopy provided important information on the proliferative potential and hemorrhaging of pituitary macroadenomas. These data may be useful for noninvasive structural monitoring of pituitary macroadenomas. Differences in the FWHMwater could be explained by iron ions of hemosiderin, which lead to worsened homogeneity of the magnetic field.

9. Neurosurgical implications of mannitol accumulation within a meningioma and its peritumoral region demonstrated by magnetic resonance spectroscopy –A case report- J Neurosurg 108:1010–1013, 2008

Mannitol is widely considered the hyperosmolar therapy of choice in routine neurosurgical practice for the reduction of intracranial pressure ICP).

The authors present a unique case of a patient with a large meningioma treated with mannitol, in which mannitol accumulation within the tumor and its surrounding parenchyma was shown using in vivo magnetic resonance spectroscopy (MRS). This rare appearance of mannitol on MRS was characterized by a wide-based peak at 3.8 ppm, which remained detectable several hours after the last dose. These findings provide the first in vivo evidence in support of the prevailing theory that mannitol leakage into the peritumoral edematous region may contribute to rebound increases in ICP and suggest that this phenomenon has the potential to occur in extraaxial tumors. Judicious use of mannitol in the setting of elevated ICP due to tumor may be indicated to avoid potentially deleterious side effects caused by its accumulation.

10. Assessment of mitochondrial impairment in traumatic brain injury using high-resolution proton magnetic resonance spectroscopy - J Neurosurg 108:42–52, 2008

The goal of this study was to demonstrate the post traumatic neurochemical damage in normal-appearing brain and to assess mitochondrial dysfunction by measuring N-acetylaspartate (NAA) levels in patients with severehead injuries, using proton (1H) magnetic

resonance (MR) spectroscopy. Semiquantitative analysis of NAA relative to creatine-containing compounds (Cr) and choline (Cho) was carried out from proton spectra obtained by means of chemical shift (CS) imaging and single-voxel (SV) methods in 25 patients with severe traumatic brain injuries (TBIs) (Glasgow Coma Scale scores # 8) using a 1.5-tesla MR unit.

Proton MR spectroscopy was also performed in 5 healthy volunteers (controls). The SV studies in patients with diffuse TBI showed partial reduction of NAA/Cho and NAA/Cr ratios within the first 10 days after injury (means 6 standard deviations 1.59 6 0.46 and 1.44 6 0.21, respectively, in the patients compared with 2.08 6 0.26 and 2.04 6 0.31, respectively, in the controls; nonsignificant difference). The ratios gradually declined in all patients as time from injury increased (mean minimum values NAA/Cho 1.05 6 0.44 and NAA/Cr 1.05 6 0.30, p , 0.03 and p , 0.02, respectively). This reduction was greater in patients with less favorable outcomes.

In patients with focal injuries, the periphery of the lesions revealed identical trends of NAA/Cho and NAA/Cr decrease.These reductions correlated with outcome at 6 months (p , 0.01). Assessment with multivoxel methods (CS imaging) demonstrated that, in diffuse injury, NAA levels declined uniformly throughout the brain. At 40 days postinjury, initially low NAA/Cho levels had recovered to near baseline

in patients who had good outcomes, whereas no recovery was evident in patients with poor outcomes (p, 0.01). Using 1H-MR spectroscopy, it is possible to detect the posttraumatic neurochemical damage of the injured brain when conventional neuroimaging techniques reveal no abnormality. Reduction of NAA levels is a dynamic process, evolving over time, decreasing and remaining low throughout the involved tissue in patients with poor outcomes. Recovery of NAA levels in patients with favorable outcomes suggests marginal mitochondrial impairment and possible resynthesis from vital neurons.

11. Proton MR Spectroscopy of Pediatric Cerebellar Tumors - AJNR Am J Neuroradiol 16:1821–1833, October 1995

This study was done to investigate the role of proton MR spectroscopy in pediatric cerebellar tumor diagnosis.

Single voxel pulse sequences with long echo time (135 or 270 milliseconds, voxel size 8 to 19 cm3), were used to obtain proton spectra of primary pediatric cerebellar tumors. Eleven primitive neuroectodermal tumors (patient age, 2 to 12 years; mean, 7 years), 11 low-grade astrocytomas (age, 2 to 16 years; mean, 9 years), 4 ependymomas (age, 1 to 6 years; mean, 4 years), 1 mixed glioma ependymo-astrocytoma (age, 11 years), 1 anaplastic ependymoma (age, 7 years), 1 ganglioglioma (age, 14 years), and 1 malignant teratoma (age, 6 days) were studied. Control cerebellum spectra were acquired from five patients without abnormality

in cerebellum (age, 2 to 15 years; mean, 8 years). The signal intensities from choline-containing compounds (Cho), creatine/phosphocreatine (Cr), *N*-acetyl-aspartate (NAA), and lactate (Lac) were quantified. The mean and standard deviation of metabolite ratios were calculated.

The control spectra ratios (NAA:Cho 5 1.49 6 0.36, Cr:Cho 5 1.13 6 0.23) were distinct from the tumor spectra (NAA:Cho 5 0.41 6 0.27 and Cr:Cho 5 0.37 6 0.23). Most of primitive neuroectodermal tumors had low NAA:Cho (0.17 6 0.09) and Cr:Cho (0.32 6 0.19). Compared with primitive neuroectodermal tumors, low-grade astrocytomas and ependymomas had higher NAA:Cho ratio (0.63 6 0.19 and 0.39 6 0.12). The Cr:Cho ratio was higher for ependymomas (0.60 6 0.20) than for astrocytomas (0.27 6 0.12) and primitive neuroectodermal tumors. No NAA was found in the malignant teratoma. Lac:Cho ratio was 0.66 6 0.40, 0.58 6 0.30, and 0.08 6 0.12 for astrocytoma, ependymoma, and primitive neuroectodermal tumor, respectively. Lactate was elevated in the mixed glioma ependymo-astrocytoma, ganglioglioma, and teratoma. The NAA and lactate signals were sometimes obscured by lipids in the spectra. Discriminant analysis was carried out using NAA:Cho and Cr:Cho ratios to differentiate the three major tumor types. The sensitivity/ specificity values for diagnosing astrocytoma, ependymoma, and primitive neuroectodermal tumor were found to be 0.91/0.84, 0.75/0.92, and 0.82/0.89, respectively, based on this study.

In many cases, proton MR spectroscopy can be used to help differentiate cerebellarprimitive neuroectodermal tumor, low-grade astrocytoma, and ependymoma.

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